Emerging Viruses

20

Abstract

Emerging viruses are viruses that appear suddenly in the human population. These are viruses to which man has no history of exposure and thus no or limited immunity; they are not new evolutionary creations, but are viruses than man meets due to environmental changes, such as deforestation, entering into new habitats, or viruses that are transmitted from one species of animal to humans. Most of these viruses are terrifying, and cause hemorrhagic fever, a complete destruction of the circulation system; they include Lassa fever, Nipah virus, Ebola, HIV, Severe acute respiratory syndrome (SARS), and, recently, Middle East respiratory syndrome (MERS), which is the latest in a series of "new" respiratory viruses infecting man. It is possible that unknown emerging viruses are the cause of death, often listed as "death due to an unknown cause," as in the retrospective cases of HIV. Emerging viruses might also include poliovirus and influenza, since their introduction into the human population is (was) often sudden and due to changes in the environment or due to contact with other animal species. For examples, polio was a result of changes in sanitation in the countries of North America and Western Europe, and influenza is constantly jumping from aquatic birds to man and other animal species where genomic reassortment occurs.

20.1 Nipah and Hendra Viruses

An interesting constituent of epidemiology is the detective work to track down the origins of novel viruses. An example of such investigative work is the exploration into the origin of Nipah virus, a paramyxovirus, which caused an epidemic illness in Malaysia in 1998. A mild disease occurred among pigs that eventually spread as a severe, fatal disease to man and dogs. The first outbreak was noted in 1998 in the

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Fig. 20.1 Grey headed flying fox (fruit bat)

village of Ampang, where there were a number of cases of fatal encephalitis among farmers, and respiratory infections and encephalitis among pigs. The disease spread to other parts of Malaysia with the movement of pigs for commercial reasons. The outbreak was arrested by a mass cull, which began on March 20, 1999 and ended on April 26 of that year, with a ban on the movement of pigs [1, 2]. Malaysia had 2.4 million pigs and 1,800 pig farms in January 1999; by July 21, 1.1 million pigs and 956 farms had been destroyed and 48 more pig farms had closed. In 1998 and 1999, there was a total of 265 confirmed human cases of Nipah virus and 105 human deaths. Infection with Nipah virus was associated with encephalitis (inflammation of the brain), characterized by fever, drowsiness, and more serious central nervous system symptoms, such as coma, seizures, and inability to breathe. The virus also spread to cats, dogs, and even to ponies. There have been no further outbreaks in Malaysia since then.

Other outbreaks of Nipah virus have occurred in humans in Bangladesh in 2004, with 75 % fatalities, [3] and in India. At the time of this outbreak, there was no evidence of human-to-human transmission. The outbreak was not associated with pigs, but with the consumption of date palm sap that had been contaminated with fruit-bat droppings. A more severe outbreak occurred in 2012 in Bangladesh where there was evidence of human-to-human transmission, and transmission through fomites or the handling of the dead bodies [4]. From 2001 to 2012 there were 280 cases of Nipah virus infections in humans, with 211 deaths—a mortality rate of 75 %.

Where did this virus come from and how did it arise? In some cases these outbreaks have been associated with land clearing for agricultural purposes. The affected area of Malaysia had been cleared of jungle and planted with fruit trees. These fruit trees were attractive to a particular species of bats known as "flying foxes (Fig. 20.1)". They in turn sprinkled the areas with their droppings into areas foraged by pigs; the droppings contained the virus, which was infectious to pigs and other mammals. Although the bats contained viral antigens and antibodies, they were healthy. Thus there was a chain of events, triggered by land clearing, that resulted in a novel virus infection. In fact, it has been hypothesized that the

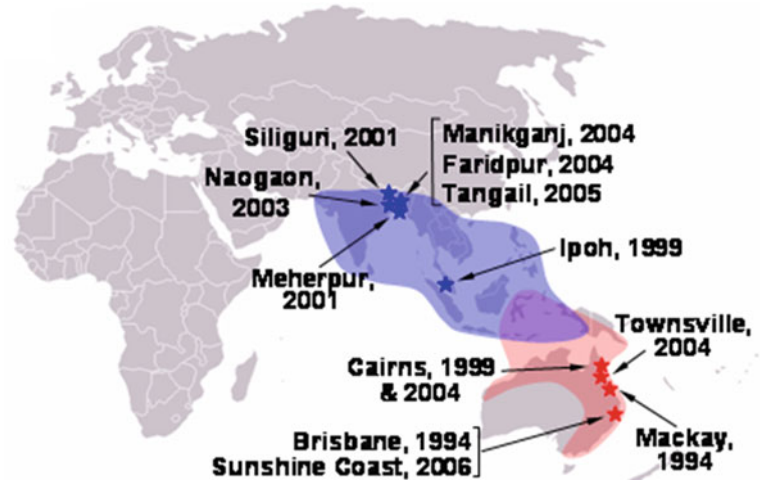

Fig. 20.2 Geographic distribution of Henipavirus outbreaks and fruit bats (*pteropodidae*)

clearing of virgin forests, as is being done in the Amazon, may also result in new infections in man as wildlife attempts to find new habitats.

A similar related virus, Hendra virus (Hendra is a suburb of Brisbane, Australia), affected horses, pigs, and livestock in Australia. There have been a number of occurrences confined to horses, and to three humans working with horses. Two of the three humans infected had respiratory illness with severe flu-like symptoms and died. (For more information see http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/nipah.htm.)

Both of these viruses are paramyxoviruses belonging to a new genus called henipavirus. The Hendra virus was first isolated in 1996, and the Nipah virus in 1999. Figure 20.2 shows the range of spread of *Pteropus* (flying fruit bats) and the sites of outbreaks of Nipah virus and Hendra virus. The National Institute of Allergy and Infectious Diseases (NIAID) has developed an effective vaccine against both viruses.

20.2 Ebola Virus

Ebola outbreaks occur with ferocity and suddenness, and with high mortality; they may originate from bats, and the virus spreads easily to a susceptible human population. Ebola is the most lethal human viral infection known, First identified in 1976 in Zaire and the Sudan, it causes hemorrhagic fever (internal bleeding) with a mortality rate of 88 %. The first recorded outbreak killed 280 out of 318 cases in Zaire, and 151 out of 284 cases in the Sudan. The disease spread very rapidly among

Table 20.1 Cases of Ebola Hemorrhagic fever in Africa, 1976–2012. http://www.cdc.gov/vhf/ebola/resources/distribution-map.html

Country	Town	Cases	Deaths	Species	Year
Dem. Rep. of Congo	Yambuku	318	280	*Zaire ebolavirus*	1976
South Sudan	Nzara	284	151	*Sudan ebolavirus*	1976
Dem. Rep. of Congo	Tandala	1	1	*Zaire ebolavirus*	1977
South Sudan	Nzara	34	22	*Sudan ebolavirus*	1979
Gabon	Mekouka	52	31	*Zaire ebolavirus*	1994
Ivory Coast	Tai Forest	1	0	*Taï Forest ebolavirus*	1994
Dem. Rep. of Congo	Kikwit	315	250	*Zaire ebolavirus*	1995
Gabon	Mayibout	37	21	*Zaire ebolavirus*	1996
Gabon	Booue	60	45	*Zaire ebolavirus*	1996
South Africa	Johannesburg	2	1	*Zaire ebolavirus*	1996
Uganda	Gulu	425	224	*Zaire ebolavirus*	2000
Gabon	Libreville	65	53	*Zaire ebolavirus*	2001
Republic of Congo	Not specified	57	43	*Zaire ebolavirus*	2001
Republic of Congo	Mbomo	143	128	*Zaire ebolavirus*	2002
Republic of Congo	Mbomo	35	29	*Zaire ebolavirus*	2003
South Sudan	Yambio	17	7	*Zaire ebolavirus*	2004
Dem. Rep. of Congo	Luebo	264	187	*Zaire ebolavirus*	2007
Uganda	Bundibugyo	149	37	*Bundibugyo ebolavirus*	2007
Dem. Rep. of Congo	Luebo	32	15	*Zaire ebolavirus*	2008
Uganda	Luwero District	1	1	*Sudan ebolavirus*	2011
Uganda	Kibaale District	11*	4*	*Sudan ebolavirus*	2012
Dem. Rep. of Congo	Isiro Health Zone	36*	13*	*Bundibugyo ebolavirus*	2012
Uganda	Luwero District	6*	3*	*Sudan ebolavirus*	2012

* Numbers reflect laboratory confirmed cases only

hospital personnel treating the sick, and among the general population through contact with ill persons, handling the dead, and reuse of needles. Because there is a danger of infection in preparing the dead for burial, there arose the practice of burning the bodies and the huts where the victims had lived; therefore, strict precautions are necessary for handling Ebola infections. A subtype of Ebola, known as Ebola Reston, occurred among monkeys imported from the Philippines in the state of Virginia and later in Texas, in 1990 and 1992. Luckily this strain was non-pathogenic for humans although some handlers did develop antibodies to the virus [5, 6]. During the 1990s there were fatal outbreaks of Ebola in the Congo; in one case, 16 people became sick from eating a chimpanzee found dead in the jungle. Other cases have involved an index case among hunters and among people associated with hunting

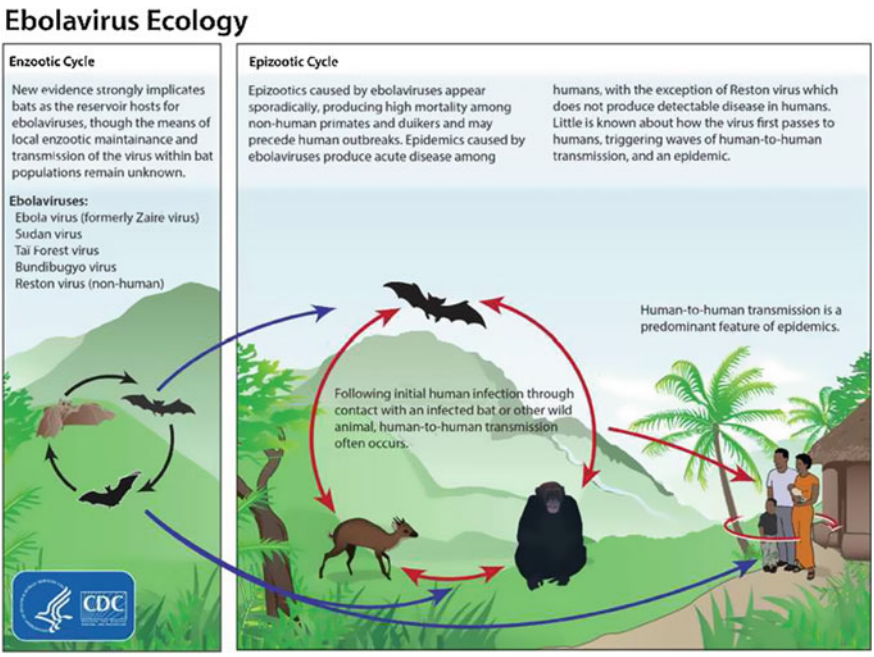

Fig. 20.3 The ecology of Ebola virus (CDC). This graphic shows the life cycle of the ebolavirus. Bats are strongly implicated as both reservoirs and hosts for the ebolavirus. Of the five identified ebolavirus subtypes, four are capable of human-to-human transmission. Initial infections in humans result from contact with an infected bat or other wild animal. Strict isolation of infected patients is essential to reduce onward ebolavirus transmission

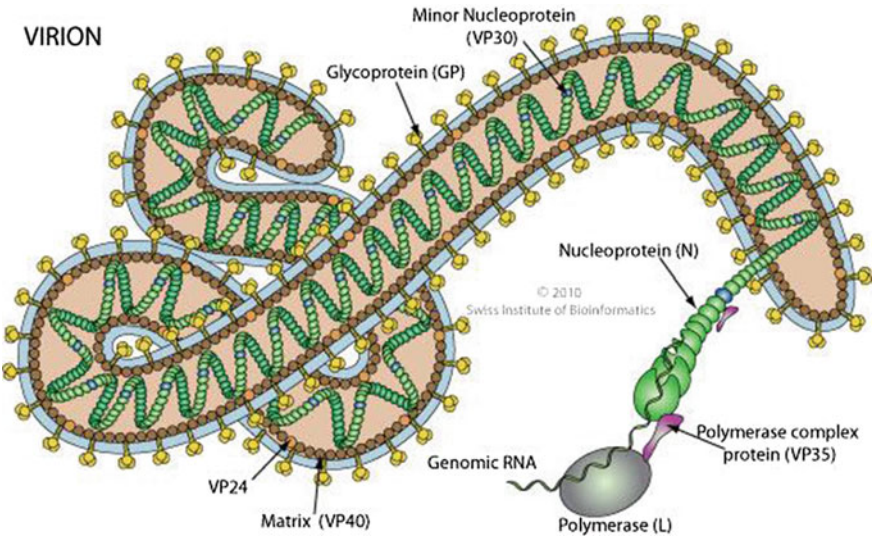

Fig. 20.4 Schematic of Ebola virus (ViralZone, SIB Swiss Institute of Bioinformatics)

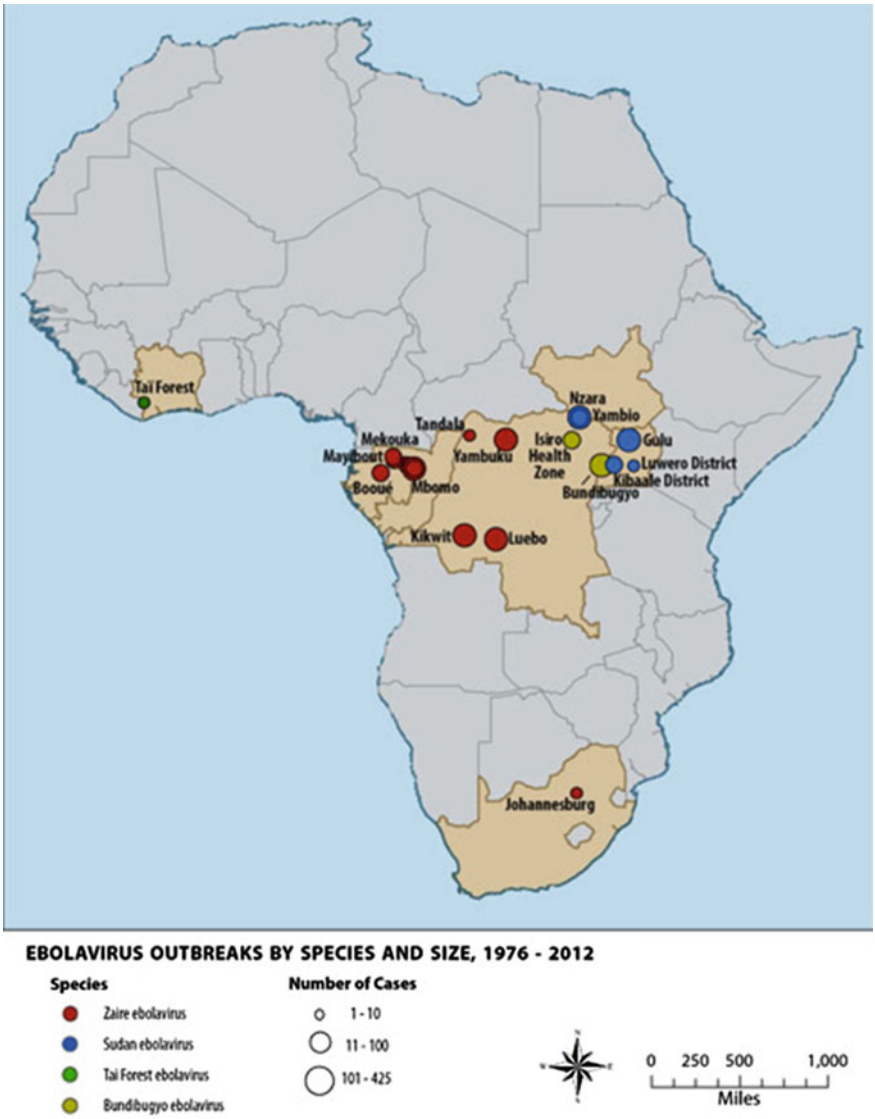

Fig. 20.5 Distribution of Ebola outbreaks in Africa (WHO)

primates. Sizeable outbreaks occurred in Uganda in 2000–2001, with 425 cases and a mortality rate of 53 %. Table 20.1 lists the major outbreaks since 1976 (source: CDC Ebola resources) (Fig. 20.3 illustrates the ecology as known, of the virus and Fig. 20.4 illustrates the unusual structure of the virus).

The three most important risks associated with Ebola virus infection were attending funerals of Ebola patients, having contact with the sick in one's family, and providing medical care to Ebola patients without using adequate personal

protective measures [7, 8]. At the time of this writing (2014), there are outbreaks of Ebola in the Congo and Uganda. The disease also infects and is fatal for non-human primates such as monkeys, gorillas and chimpanzees. According to the CDC and WHO, the zoonose origin of Ebola is still unknown, although bats are suspect in this case and also in a similar disease, Marburg hemorrhagic fever. Figure 20.5 presents the distribution of Ebola on the African continent.

Ebola virus belongs to a family of viruses known as "filoviruses." This is a long, 970 nm filamentous negative-stranded RNA virus (Fig. 20.2). The viral proteins inhibit interferon activity. The viral RNA codes for 7–8 proteins.

20.3 SARS

SARS first appeared in 2002. Between November 2002 and July 2003 there were approximately 800 cases in southern China, with a death toll of 10 %. The major "hot spot" was Hong Kong, with 9 % fatality, but within a few months SARS spread worldwide, carried by unsuspecting travelers. The range and the speed of worldwide transmission are very well documented. (A day-to-day account of the epidemic is presented both at http://www.cdc.gov/about/history/sars/timeline.htm and http://en.wikipedia.org/wiki/Progress_of_the_SARS_outbreak.)

In the days before air transport, it may have been confined to this area of southern China.

The infectious virus was identified as a coronavirus in 2003 (Fig. 20.6).

SARS typically begins with flu-like signs and symptoms—fever, chills, muscle aches and occasionally diarrhea. After about a week, signs and symptoms include fever of 100.4 °F (38 °C) or higher, dry cough, and shortness of breath.

The SARS epidemic (or pandemic) showed how quickly infection can spread in a highly mobile and interconnected world. The SARS epidemic also showed how international cooperation among health care experts can effectively contain the

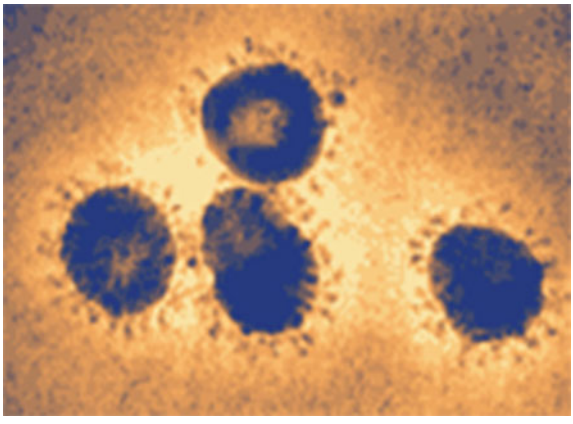

Fig. 20.6 Electron micrograph image of SARS (http://www.cdc.gov/niosh/topics/SARS)

spread of the disease. Since 2004, known instances of SARS transmission have fallen to zero worldwide.

The virus spread from southern China to Singapore, Taiwan, the U.S. and Canada (Ontario). To date, there is no vaccine against SARS; however, the passive transfer of antibodies inhibits the virus. If an outbreak is suspected, patients should be quarantined, and a strict regimen of sterility enforced. Most important is for health care workers to avoid contact with the patients, to wear surgical masks, and to regularly wash their hands.

The detective work involved in tracking the SARS epidemic is fascinating in its extensiveness and detail. Every case appears to have been followed and documented (see references to CDC and Wikipedia above).

The first case of SARS appeared to have been a farmer from the Guangdong area of China (that borders Hong Kong). The Chinese authorities reported the outbreak to the WHO, with 305 cases (including 105 health care workers) and five deaths. This may have been an underestimate of the severity of the outbreak [9]. The first clue of the outbreak appears to be on November 27, 2002, when Canada's Global Public Health International Network (GPHIN), an electronic warning system that is part of the World Health Organization's Global Outbreak and Alert Response Network (GOARN), picked up reports of a "flu outbreak" in China through Internet media monitoring and analysis, and the data was forwarded to the WHO. Most news media in China did not report the extent of the outbreak, in keeping with the government's policy of not reporting bad news. This hindered the treatment and the recognition that this was a major new epidemic illness. The illness spread extremely quickly, primarily among health care workers and physicians attending to the sick. What is rather amazing is the speed with which the virus was sequenced, recognized, and brought under control by quarantine and international cooperation. Scientists are still puzzled as to how 64-year-old Dr. Liu Jianlun could have transferred—during his brief stay—the virus to 16 other occupants of the same floor of his hotel. These guests subsequently travelled to other destinations, including Toronto, Vietnam, and Singapore, thus spreading the virus. In less than 4 months, some 4,000 cases and 550 deaths from SARS outside of China can be traced to this one visit to the Metropol Hotel. (The hotel is considering turning the 9th floor, where Dr. Jianlun stayed, into a museum.) [10].

It took about 5 months from the initial outbreak for the Chinese authorities to allow physicians from the WHO to visit Guodong province, and to admit to the seriousness of the epidemic. Once admitted, the Chinese authorities carried out Draconian measures to bring the infection under control, even firing the mayor and health minister in Beijing. This was followed by mass quarantine of hospital wards, under armed guards, and threat of execution of anyone knowingly having SARS and avoiding quarantine. However, these measures and international cooperation stopped the epidemic from spreading.

SARS did have grave economic consequences. It substantially damaged the tourist trade in Hong Kong and Taiwan as well as in Toronto. Taiwan in part blamed the recession in that island on the SARS outbreak (Fig. 20.7).

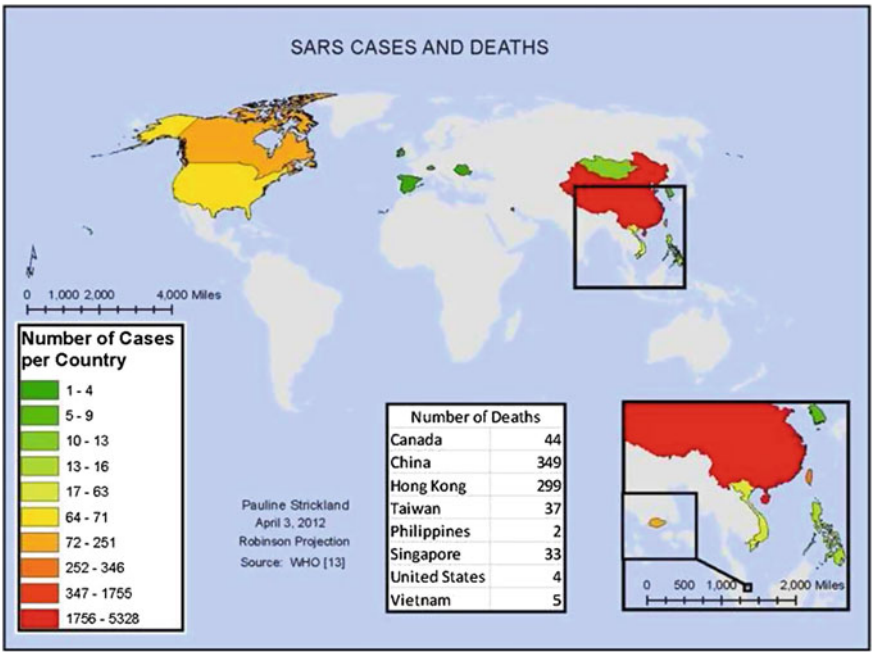

Fig. 20.7 Distribution of SARS cases and deaths. http://en.wikipedia.org/wiki/File:Sars_Cases_and_Deaths.pdf

The identification of the virus occurred rapidly following the initial outbreak of the infection. The isolate (initially unknown whether viral or not, but at one time suspected of being *Chlamydia*) [9] was grown in culture and tested against sera from recovering individuals and uninfected controls. The virus was inhibited by their sera, thus allowing for a diagnostic test to be developed. However, at this early stage it was impossible to identify the virus. The virus was later identified as a previously unknown corona virus. Corona viruses normally cause symptoms of a cold, and take about 10 days' incubation to manifest. In this case, the long incubation period helped the spread of the virus.

Where did the virus come from? Initial testing indicated that the virus came from civets (a member of the cat family), a food delicacy in China and found in the open markets. Further analysis of civets in the wild did not find traces of the virus. Thus the civets in the market must have also been "dead-end" victims of SARS. In 2005 two teams of researchers reported the presence of similar corona viruses in Chinese horseshoe bats. These are probably the culprits, and the virus was probably passed on through an intermediate host in the market. Using DNA sequencing techniques (although this is an RNA virus), scientists have been able to work out the relationship between the virus discovered in humans, bats, and civets [11, 12].

There seems to be no doubt that bats carry many species of corona viruses similar in sequence to SARS. A phylogenic tree shows that civet and human SARS viruses are very similar and, most importantly, that both are nested within a *clade* of bat viruses—so the ancestor of the civet and human strains seems to have been a bat virus! Based on this evidence, biologists have come up with a plausible path of transmission: infected bats and uninfected civets came into contact at a market, the virus was transmitted to civets and then multiplied and evolved in civets (or other animals) in the public market, until eventually the virus hopped over to humans. It is apparent that many of the "emerging" viruses can be linked back to bats (including Nipah and possibly Ebola viruses).

20.4 Middle East Respiratory Syndrome Virus

Since September 2012 another virus (HCoV-EMC/2012, later known as MERS, for MERS virus, has been affecting people in Saudi Arabia, Qatar, nearby countries, and even some European countries [13]. As of this writing (March 2014), MERS has infected 186 people and killed 81. It appears to be a corona virus related to SARS, causing severe pneumonia and kidney failure. Part of the virus has been sequenced and compared with other corona viruses. Once again, this virus appears to have originated in bats and spread to humans, either directly or through an intermediate host. Bats in Saudi Arabia contain many different corona viruses. It was possible to isolate a virus with nucleotide sequences identical to that in an infected patient in one case [14]. The virus does appear in clusters and there is human-to-human transmission. The fatality rate is high—over 30 %. It has been traced to an Egyptian tomb bat, with the sequence of the viral RNA identical to that of the index case.

Thus, this virus appears to be genetically related to the SARS virus. Recent evidence suggests that dromedary camels found in southern Oman may have also been infected in the past with the MERS virus, since antibodies to components of the virus have been found in the sera of such animals, but there is no evidence that this is the source of the current epidemic.

20.5 HantaVirus

Hantavirus causes a severe respiratory infection and is transmitted by a variety of different rodents, mostly mice. The name comes from the Hantan River in South Korea. The virus caused an outbreak of hemorrhagic fever among American and Korean troops during the Korean War of 1951–1953, with more than 3,000 troops being sick with kidney failure and internal bleeding; the mortality rate was 10 %. The virus was not isolated until 1976 and found in a striped field mouse [15] and urban rats.

This disease was first recognized in the U.S. (Four Corners Disease) in 1993. An unexplained pulmonary (lung) illness occurred in an area shared by Arizona, New Mexico, Colorado and Utah. Quite a number of previously healthy young

Fig. 20.8 Cotton rat. The cotton rat, *Sigmodon hispidus*, is a Hantavirus carrier that becomes a threat when it enters human habitation in rural and suburban areas

adults died from an acute respiratory infection; the outbreak was related to an increase in crop yield with a concomitant increase in the deer mouse population. The virus was isolated from a deer mouse captured close to the home of one of the victims, and identified as a new virus, first called "Muerto Canyon virus," but later changed to "Sin Nombre virus" (SNV). Why did this outbreak occur in 1993? Previous years had seen periods of drought, and not enough food to maintain a large deer mouse population. In 1993 there was plenty of rain and snow, and thus the plant yield was greater than usual. It is estimated that the deer mouse population grew tenfold during this period, and thus had more contact with humans [16]. Since the initial outbreak of Hantavirus, other strains of the virus have been identified that have not been associated with the Four Corners states [17]. This is probably not a new virus; the Navajo Indians of the region appeared to be familiar with a respiratory infection that was associated with increases in the mouse population. Certain strains of Hantavirus can be transmitted between humans.

Hantaviruses have now been identified in large areas of the U.S., all carried by different rodents. [These rodents are described in http://www.cdc.gov/hantavirus/rodents/white-footed-mouse.html (Fig. 20.8).]

Since November 2012 there have been 10 confirmed cases of Hantavirus infection in Yosemite National Park, with three fatalities. From the CDC website: "NPS public health officials believe that 9 of the 10 people with confirmed hantavirus infection were exposed to the virus while staying at the Signature Tent Cabins in Curry Village in Yosemite National Park. The other park visitor with Hantavirus infection was probably exposed to the virus while hiking or staying at the High Sierra Camps, located about 15 miles from Curry Village. Some of the infected cabins have now been destroyed." (An interesting article on the Yosemite outbreak can be found at http://www.outsideonline.com/adventure-travel/north-america/united-states/national-parks/Death-at-Yosemite-The-Story-Behind-Last-Summers-Hantavirus-Outbreak.html.)

The Hantavirus belongs to the family of *Bunyaviridae*, a single-stranded RNA virus with a segmented genome. The virus encodes four to six proteins.

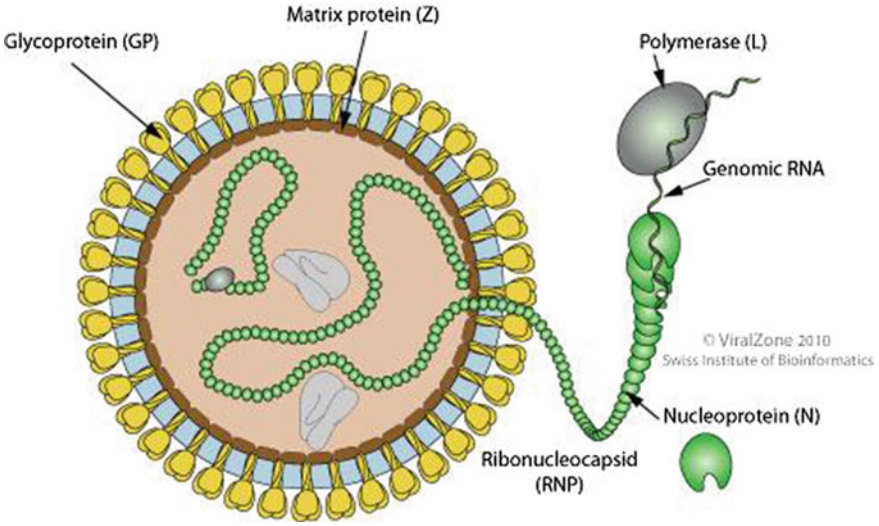

Fig. 20.9 Schematic of an arenavirus. Note that there are two separate strands of RNA (ViralZone, SIB Swiss Institute of Bioinformatics)

20.6 Lassa Fever

There are many other types of hemorrhagic fever viruses, not as lethal as Ebola, but still very dangerous. These include the arena viruses, a large class of viruses that include Lassa fever, and other hemorrhagic fever viruses named for their countries of origin, such as Bolivian, Venezuelan, and Brazilian hemorrhagic fevers; these viruses are associated with rats and mice (Fig. 20.9). They do not cause obvious illness in the rodent population and the virus is shed in the urine or droppings of the rodents. The virus can be inhaled as an aerosol, or in some cases transferred by person-to-person contact, as discussed above for Ebola. Lassa virus was first identified in 1969 when two missionary nurses died in Nigeria, West Africa. The virus causes significant morbidity and mortality. It is endemic in western Africa and the estimates are of between 100,000 and 300,000 infections per year. The mortality rate varies between 5–25 %, depending on the outbreak. Many more may be infected without symptoms. The reservoir, or host, of Lassa virus is a rodent known as the "multimammate rat" of the genus *Mastomys*. This is a small rat that lives among humans in large areas of West, Central and East Africa. The virus is spread in the droppings and urine of the rats, and may be picked up in dust. The rats are often consumed as food, and if infected, transmission to humans may occur during handling. Human-to-human transmission may also occur through body fluids and sexual transmission, since the virus can be found in semen. Eradicating the rats, storing food in rodent-proof containers, trapping and removing the animals and avoiding them for food, can control the

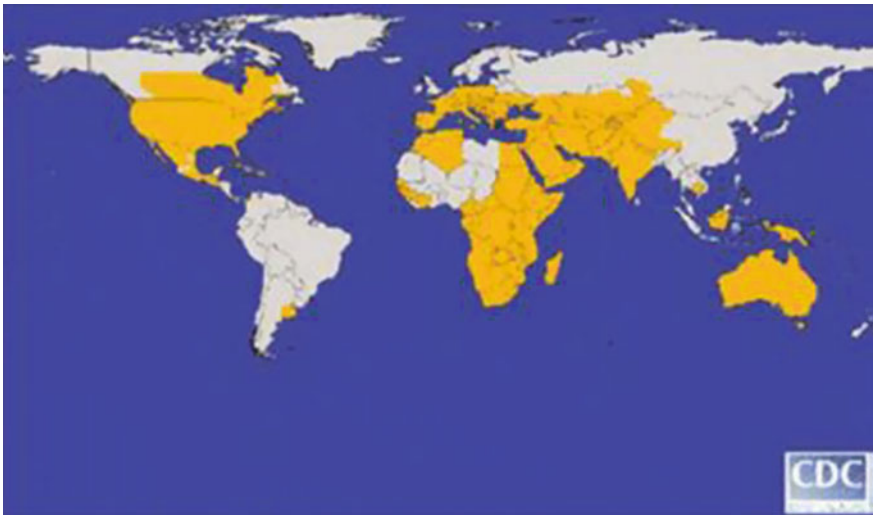

Fig. 20.10 Global distribution of West Nile virus (CDC)

virus. However, the population of rats is so great that annihilation of the population is very difficult.

Lassa fever belongs to the genus of viruses known as "arenavirus." Five arenaviruses are known to cause human illness: Lassa virus, Junin virus, Machupo virus, Guanarito virus and Sabia virus. The structure of the nucleic acid is rather unusual, in that it is segmented, each piece of opposite polarity. Both segments are ambisense. The viral RNA-dependent RNA polymerase (L) binds to a promoter on each encapsidated segment, and transcribes a messenger RNA. Transcription is terminated by a strong hairpin sequence at the end of each gene. mRNAs are capped, probably by L protein during synthesis. An ambisense genome is one in which both nucleic acid strands encode for proteins (Fig. 20.9).

20.7 West Nile Virus

Mosquitoes or other insects transmit many "emerging" viruses. Recently there have been outbreaks in the U.S. of West Nile virus, a virus carried by mosquitoes and transmitted to birds and often to humans. West Nile virus was first isolated from a feverish woman in the West Nile District of Uganda in 1937. The ecology was characterized in Egypt in the 1950s. The virus became recognized as a cause of severe human meningitis or encephalitis (inflammation of the spinal cord and brain) in elderly patients during an outbreak in Israel in 1957. An equine form of the disease was first noted in Egypt and France in the early 1960s. WNV first appeared in North America in 1999, with encephalitis reported in humans and horses. Since then there have been a large number of cases of WNV in birds and in

Table 20.2 Number of incidents of West Nile virus by state (USA) from 1999–2012

West Nile virus disease cases reported to CDC by state, 1999–2012 State	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	Total
Alabama	0	0	2	49	37	16	10	8	24	18	0	3	5	62	234
Alaska	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Arizona	0	0	0	0	13	391	113	150	97	114	20	167	69	133	1,267
Arkansas	0	0	0	43	25	28	28	29	20	9	6	7	1	64	260
California	0	0	0	1	3	779	880	278	380	445	112	111	158	479	3,626
Colorado	0	0	0	14	2,947	291	106	345	576	71	103	81	7	131	4,672
Connecticut	0	1	6	17	17	1	6	9	4	8	0	11	9	21	110
Delaware	0	0	0	1	17	0	2	0	1	1	0	0	1	9	32
Dist. of Columbia	0	0	0	34	3	2	5	2	0	8	2	6	15	10	87
Florida	0	0	12	28	94	41	21	3	3	3	3	12	24	73	317
Georgia	0	0	6	44	50	21	20	8	50	8	4	13	22	99	345
Hawaii	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Idaho	0	0	0	0	1	3	13	996	132	39	38	1	3	17	1,243
Illinois	0	0	0	884	54	60	252	215	101	20	5	61	34	290	1,976
Indiana	0	0	0	293	47	13	23	80	24	4	4	13	9	77	587
Iowa	0	0	0	54	147	23	37	37	30	6	5	9	9	31	388
Kansas	0	0	0	22	91	43	25	30	40	31	13	19	4	56	374
Kentucky	0	0	0	75	14	7	5	6	4	3	3	3	5	23	148

(continued)

Table 20.2 (continued)

West Nile virus disease cases reported to CDC by state, 1999–2012 State	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	Total
Louisiana	0	0	1	329	124	109	171	180	40	49	21	27	10	335	1,396
Maine	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Maryland	0	0	6	36	73	16	5	11	10	14	1	23	19	47	261
Massachusetts	0	0	3	23	17	0	6	3	6	1	0	7	6	33	105
Michigan	0	0	0	614	19	16	62	55	17	17	1	29	34	202	1,066
Minnesota	0	0	0	48	148	34	45	65	101	10	4	8	2	70	535
Mississippi	0	0	0	192	87	51	70	183	136	65	53	8	52	247	1,144
Missouri	0	0	0	168	64	36	30	62	77	15	5	3	10	20	490
Montana	0	0	0	2	222	6	25	34	202	5	5	0	1	6	508
Nebraska	0	0	0	152	1,942	53	188	264	163	47	52	39	29	193	3,122
Nevada	0	0	0	0	2	44	31	124	12	16	12	2	16	9	268
New Hampshire	0	0	0	0	3	0	0	0	0	0	0	1	0	1	5
New Jersey	0	6	12	24	34	1	6	5	1	10	3	30	7	48	187
New Mexico	0	0	0	0	209	88	33	8	60	8	8	25	4	47	490
New York	62	14	15	82	71	10	38	24	22	46	7	128	44	107	670
North Carolina	0	0	0	2	24	3	4	1	8	3	0	0	2	7	54
North Dakota	0	0	0	17	617	20	86	137	369	37	1	9	4	89	1,386
Ohio	0	0	0	441	108	12	61	48	23	15	2	5	21	121	857

(continued)

Table 20.2 (continued)

West Nile virus disease cases reported to CDC by state, 1999–2012 State	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	Total
Oklahoma	0	0	0	21	79	22	31	48	107	9	10	1	1	191	520
Oregon	0	0	0	0	0	3	7	69	26	16	11	0	0	11	143
Pennsylvania	0	0	3	62	237	15	25	9	10	14	0	28	6	60	469
Puerto Rico	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Rhode Island	0	0	0	1	7	0	1	0	1	1	0	0	1	4	16
South Carolina	0	0	0	1	6	2	5	1	5	1	3	1	0	29	54
South Dakota	0	0	0	37	1,039	51	229	113	208	39	21	20	2	203	1,962
Tennessee	0	0	0	56	26	14	18	22	11	19	9	4	18	33	230
Texas	0	0	0	202	720	176	195	354	260	64	115	89	27	1,868	4,070
Utah	0	0	0	0	1	11	52	158	70	26	2	2	3	5	330
Vermont	0	0	0	1	3	0	0	0	0	0	0	0	1	3	8
Virginia	0	0	0	29	26	5	1	5	5	1	5	5	9	30	121
Washington	0	0	0	0	0	0	0	3	0	3	38	2	0	4	50
West Virginia	0	0	0	3	2	0	0	1	0	1	0	0	2	10	19
Wisconsin	0	0	0	52	17	12	17	21	13	8	1	2	3	57	203
Wyoming	0	0	0	2	375	10	12	65	181	8	12	6	3	7	681
Total	62	21	66	4,156	9,862	2,539	3,000	4,269	3,630	1,356	720	1,021	712	5,674	37,088

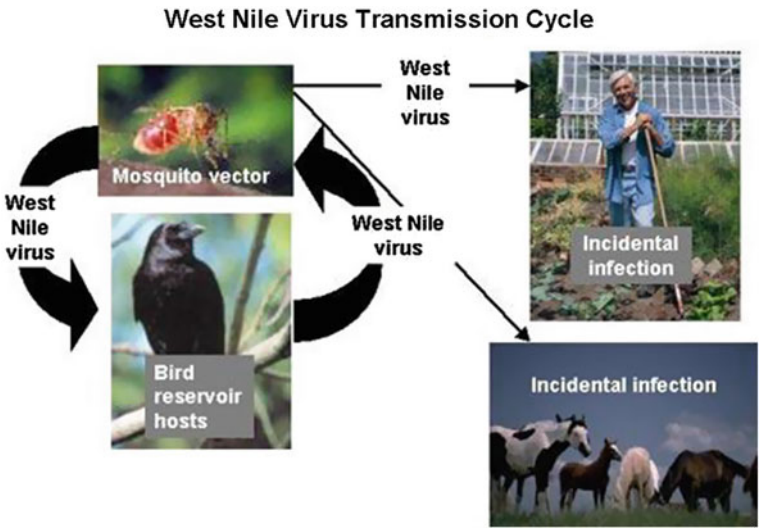

Fig. 20.11 West Nile transmission cycle. Note that man and horse are "dead-end" hosts (http://www.cdc.gov/westnile/index.html)

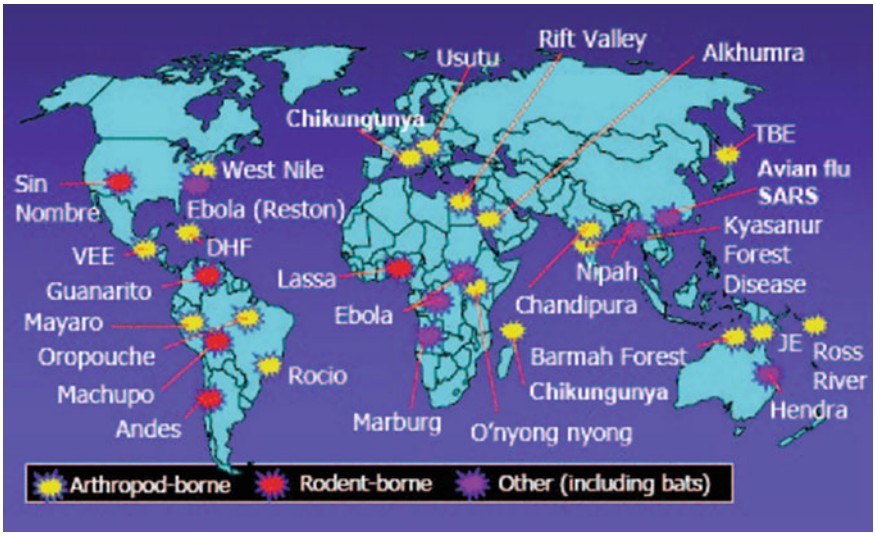

Fig. 20.12 Map of emerging viruses showing the animal reservoir, or the vector (American Medical Veterinary Association)

humans, and it is now considered one of the most widespread of the "emerging viruses." The virus has now spread globally with new strains being identified in 2012 (Fig. 20.10).

The virus is transmitted in a bird-mosquito cycle, with humans being considered dead- end hosts (Fig. 20.11). The major birds infected include the American crow, blue jays, black-billed magpies, and less commonly, robins and house sparrows. West Nile virus is a reportable infection and the CDC has tracked the number of cases in humans according to state (Table 20.2).

Numbers fluctuate from year to year after a large increase in 2002. In 2012, Texas had the most cases. The virus is carried by birds and transmitted by mosquitoes. It is estimated that 20 % of the people who become infected will develop West Nile fever, leaving 80 % of those infected not experiencing any type of illness. It is also estimated that 1 in every 150 persons infected with West Nile virus will develop a more severe form of the disease. In 2012 the virus killed 286 people in the U.S., with Texas being the hardest hit. Those who survive encephalitis may have permanent neurological damage. The virus has been found in almost all rodents in the U.S., so when controlling this disease it is important to control mosquito populations. It is also important to wear protective clothing and to spray clothing and the body with mosquito repellent. West Nile virus is not transmitted from human to human (see Fig. 20.5); it is a *flavivirus*, the same class as yellow fever and hepatitis C. Its mode of replication is similar to that of those two viruses. Figure 20.12 is a summary figure of the known emerging viruses as of 2012.

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